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ARTICLES

The germfree state prevents development of gut and joint inflammatory disease in HLA-B27 transgenic rats

JD Taurog, JA Richardson, JT Croft, WA Simmons, M Zhou, JL Fernandez-Sueiro, E Balish and RE Hammer

Harold C. Simmons Arthritis Research Center, University of Texas Southwestern Medical Center, Dallas 75235.

A number of inflammatory disease states occur with greatly increased frequency in individuals inheriting the human major histocompatibility complex class I allele HLA-B27. In a minority of cases, namely those with B27-associated reactive arthritis, there is good evidence that the disease state is triggered by infection with an enteric or genitourinary bacterial pathogen. For the majority of B27-associated disease, no definite pathogenetic role for bacteria has been established. However, in these latter cases intestinal inflammation can often be demonstrated, and it sometimes occupies a major part of the clinical picture. Rats transgenic for B27 are known to develop a disorder resembling B27-associated human disease, with prominent intestinal, joint, skin, and male genital inflammatory lesions. We report here that B27 transgenic rats raised in a germfree environment do not develop inflammatory intestinal or peripheral joint disease, whereas the skin and genital inflammatory lesions are unaffected by the germfree state. These findings support the concept that gut and joint inflammation are pathogenetically closely related, and they provide direct evidence that the commensal gut flora play an important role in the pathogenesis of B27-associated gut and joint inflammation.

This article has been cited by other articles:

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- Oldstone, M. B. A. (1998). Molecular mimicry and immune-mediated diseases. *FASEB J.* 12: 1255-1265 [Abstract] [Full Text]
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L9 ANSWER 1 OF 3 MEDLINE DUPLICATE 1
AN 96281915 MEDLINE
DN 96281915
TI **HLA**-DR4-IE chimeric class II **transgenic**, murine class II-deficient mice are susceptible to experimental allergic encephalomyelitis.
AU Ito K; Bian H J; Molina M; Han J; Magram J; Saar E; Belunis C; Bolin D R; Arceo R; Campbell R; Falcioni F; Vidovic D; Hammer J; Nagy Z A
CS Department of Inflammation and Autoimmune Diseases, Hoffmann-La Roche Inc., Nutley, New Jersey 07110, USA.
SO **JOURNAL OF EXPERIMENTAL MEDICINE, (1996 Jun 1)** 183 (6) 2635-44.
Journal code: I2V. ISSN: 0022-1007.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199610
AB To investigate the development of **HLA**-DR-associated autoimmune diseases, we generated **transgenic** (Tg) mice with **HLA**-DRA-IE alpha and **HLA**-DRB1*0401-IE beta chimeric genes. The transgene-encoded proteins consisted of antigen-binding domains from **HLA**-DRA and **HLA**-DRB1*0401 molecules and the remaining domains from the IE(d)-alpha and IE(d)-beta chains. The chimeric molecules showed the same antigen-binding specificity as **HLA**-DRB1*0401 molecules, and were functional in presenting antigens to T cells. The Tg mice were backcrossed to MHC class II-deficient (IA beta-, IE alpha-) mice to eliminate any effect of endogenous MHC class II genes on the development of autoimmune diseases. As expected, IA alpha beta or IE alpha beta molecules were not expressed in Tg mice. Moreover, cell-surface expression of endogenous IE beta associated with **HLA**-DRA-IE alpha was not detectable in several Tg mouse lines by flow cytometric analysis. The **HLA**-DRA-IE alpha/**HLA**-DRB1*0401-IE beta molecules rescued the development of CD4+ T cells in MHC class II-deficient mice, but T cells expressing V beta 5, V beta 11, and V beta 12 were specifically deleted. Tg mice were immunized with peptides, myelin basic protein (MBP) 87-106 and proteolipid protein (PLP) 175-192, that are considered to be immunodominant epitopes in **HLA**-DR4 individuals. PLP175-192 provoked a strong proliferative response of lymph node T cells from Tg mice, and caused inflammatory lesions in white matter of the CNS and symptoms of experimental allergic encephalomyelitis (EAE). Immunization with MBP87-106 elicited a very weak proliferative T cell response and caused mild EAE. Non-Tg mice immunized with either PLP175-192 or MBP87-106 did not develop EAE. These results demonstrated that a human MHC class II binding site alone can confer susceptibility to an experimentally induced murine autoimmune disease.

L4 ANSWER 1 OF 3 MEDLINE DUPLICATE 1
AN 89035546 MEDLINE
DN 89035546
TI HLA-B27 in inbred and non-inbred **transgenic** mice. Cell surface expression and recognition as an alloantigen in the absence of human beta 2-microglobulin.
AU **Taurog J D**; Lowen L; Forman J; Hammer R E
CS Harold C. Simmons Arthritis Research Center, University of Texas, Dallas 75235.
NC AR38319 (NIAMS)
AI13111 (NIAID)
AI11851 (NIAID)
+
SO JOURNAL OF IMMUNOLOGY, **(1988 Dec 1)** 141 (11) 4020-3.
Journal code: IFB. ISSN: 0022-1767.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 198902
AB A gene encoding the H chain of the human class I MHC Ag HLA-B27 was introduced into the germ lines of inbred C57BL/6 (B6) and non-inbred (B6 X SJL/J) F2 mice. By immunofluorescence and flow cytometry, the HLA-B27 gene product was expressed on lymphoid cells at levels comparable to the endogenous H-2b and H-2s class I MHC molecules. In both primary and secondary MLC between responder spleen cells from non-**transgenic** (B6 X SJL/J) F1 mice and **transgenic** stimulator cells, CTL were generated that specifically lysed mouse L cell (H-2k) or human B cell targets expressing HLA-B27, and this lysis thus appeared largely unrestricted by H-2. These results indicate that **transgenic** mice express a functional HLA-B27 gene product on cell surfaces in the absence of the human beta 2-microglobulin gene. These **transgenic** mice promise to be a valuable resource in the investigation of the unique role of HLA-B27 in inflammatory human disease.

(FILE 'HOME' ENTERED AT 14:28:33 ON 05 APR 2001)

FILE 'MEDLINE, BIOSIS, CAPLUS' ENTERED AT 14:28:41 ON 05 APR 2001
E TAUROG/AU
L1 539 S E3-E11
L2 32 S L1 AND PY=1988
L3 6 S L2 AND TRANSGENIC#
L4 3 DUP REM L3 (3 DUPLICATES REMOVED)
E ITO/AU
E JOURNAL OF EXPERIMENTAL MED?/JT
L5 15470 S E4, E5
L6 1093 S L5 AND PY=1996
L7 122 S L6 AND TRANSGENIC#
L8 6 S L7 AND HLA?
L9 3 DUP REM L8 (3 DUPLICATES REMOVED)

FILE 'STNGUIDE' ENTERED AT 14:35:42 ON 05 APR 2001

FILE 'MEDLINE, BIOSIS, CAPLUS' ENTERED AT 14:39:02 ON 05 APR 2001
L10 19 S L1 AND PY=1994
L11 9 S L10 AND TRANSGENIC#
L12 7 DUP REM L11 (2 DUPLICATES REMOVED)

FILE 'STNGUIDE' ENTERED AT 14:40:53 ON 05 APR 2001
L13 1 S TRANSGENIC#

FILE 'MEDLINE, BIOSIS, CAPLUS' ENTERED AT 14:43:33 ON 05 APR 2001
L14 99873 S TRANSGENIC#
L15 1019761 S ANTIGEN#
L16 13778 S L14 AND ANTIGEN##
L17 1087 S L16 AND (HLA? OR HUMAN LEUKOCYTE ANTIGEN# OR HUMAN LYMPHOCYTE
L18 1523 S L14 AND (HLA? OR HUMAN LEUKOCYTE ANTIGEN# OR HUMAN LYMPHOCYTE
L19 1347 S L14 (P) (HLA? OR HUMAN LEUKOCYTE ANTIGEN# OR HUMAN LYMPHOCYTE
L20 55 S L19 AND (TAA# OR MART? OR MAGE? OR GP100 OR TUMOR# (5A) ANTIG
L21 5 S L20 AND (TCR OR TCRS OR T CELL RECEPTOR#)
L22 4 DUP REM L21 (1 DUPLICATE REMOVED)

FILE 'STNGUIDE' ENTERED AT 14:53:13 ON 05 APR 2001

FILE 'MEDLINE, BIOSIS, CAPLUS' ENTERED AT 14:53:36 ON 05 APR 2001
L23 50 S L20 NOT L21
L24 29 DUP REM L23 (21 DUPLICATES REMOVED)
L25 8 S L24 NOT PY>1997

FILE 'STNGUIDE' ENTERED AT 15:00:26 ON 05 APR 2001

FILE 'MEDLINE, BIOSIS, CAPLUS' ENTERED AT 15:02:57 ON 05 APR 2001